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Atty Docket: 21339-US
Serial No. 10/635,171
Response to Non-Final Action
Page 5 of 8Remarks:

Claims 1,4-10, 14, 15, and 27 are pending in the present application. By this Amendment, claim 1 is amended. No claims are canceled, and no new claims are added. Support for the amendment to claim 1 is found in the specification as originally filed, particularly in the following locations: page 11, lines 22-29; and Example 2, page 18, lines 30-33, which, as explained below, disclose a pair of primers having spacer entities consisting of A-T base pairs and no other bases. Therefore, no new matter is added to the claims by this amendment, and the amendment places the pending claims in condition for allowance. Accordingly, entry of the amendment is respectfully requested.

Claim Rejections under 35 U.S.C. 112:

Claims 1, 4-10 and 14 were rejected under 35 U.S.C. 112, first paragraph, on the ground that the specification did not appear to provide specific support for stems consisting essentially of A/T base interactions. The same claims were also rejected under 35 U.S.C. 112, second paragraph, on the ground that the specification did not particularly point out and distinctly claim the same claimed subject matter.

Without admitting to the propriety of the rejections, and solely to expedite prosecution of the application, Applicants have chosen to amend claim 1 to specifically recite that the noncovalent interactions consist of A/T base pair interactions. It is well settled that the transitional phrase "consisting of" excludes any element, step or ingredient not specified in the element to which the phrase is applied. MPEP 2111.03. Thus, because the claims recite that the spacers of the FRET hybridization probes are capable of forming noncovalent interactions with each other, and these noncovalent interactions consist of A/T base pair interactions, the claims as worded clearly exclude spacers in which G/C base pairs, or indeed any other type of noncovalent interactions, are present. Applicants respectfully submit that claims 1, 4-10 and 14 now particularly point out and distinctly claim the same claimed subject matter. Applicants reserve the right to contest the examiner's interpretation of the transitional phrase "consisting essentially of", either in a divisional application or in an appeal from the pending final rejection.

With respect to the issue of support in the specification, Applicants direct the Examiner's attention to page 11, lines 22-29, which recites,

"The first oligonucleotide is designed in such a way that 3' to the nucleotide sequence entity which is substantially complementary to the sequence of the target nucleic acid, there are 1-10, preferably 3-8, and most preferably 3-5 *additional*

nucleotide residues which act as a spacer entity...In one embodiment, the additional residues are A or T residues. In another embodiment, more than 60% of the additional residues are A or T residues. In yet another embodiment, the two or the three 3' terminal residues are A or T residues". (emphases added)

The second oligonucleotide, to which the first oligonucleotide is complementary (see page 11, lines 8-9), is described in much the same way (page 11, line 30 to page 12, line 4), and also describes an embodiment in which all the additional residues of the spacer entity, this time at the 5' end, are A or T residues.

Additionally, a spacer entity consisting entirely of A/T residues is disclosed in Example 2 (page 17). Specifically, the specification teaches that the probe of SEQ ID NO: 5 comprises a 3' terminal oligo-A pentamer, and the probe of SEQ ID NO: 6 comprises a 5' terminal oligo-T pentamer (page 18, lines 30-32). The two probes together are described as forming a FRET hybridization probe pair according to the invention (page 18, lines 32-33). The two probes hybridize to a region of the human Factor V gene. As shown in Appendix A, the oligo-A pentamer of SEQ ID NO: 5 hybridizes to the oligo-T pentamer of SEQ ID NO: 6, and there is no G or C anywhere in this stem. The yellow highlighted region of SEQ ID NO: 5, and the gray highlighted portion of SEQ ID NO: 6, show the portions of each probe that hybridizes to the target sequence of the human factor V gene. There is a C residue on the target sequence between the probes, but this does not form any part of the A/T stem. One of skill in the art, knowing the sequences given, as referenced in the specification, and having access to conventional sequence analysis tools, would easily be able to ascertain that the FRET hybridization probe pair disclosed in this example would consist only of A/T base pairs. Accordingly, the specification provides full support for such a claim element. Withdrawal of the rejections of claims 1, 4-10 and 14 under 35 U.S.C. 112, first paragraph for lack of specific support, and under 35 U.S.C. 112, second paragraph for failing to particularly point out and distinctly claim the same claimed subject matter is therefore respectfully requested.

Claim Rejections under 35 U.S.C. 102:

Claims 1, 5, 10, and 27 were rejected under 35 U.S.C. 102(b) as anticipated by US Patent 6,130,047 (Nadeau et al). While not admitting to the propriety of the rejection, and solely to expedite prosecution of the application, Applicants have chosen to amend claim 1 to recite that the spacer entities of the FRET hybridization probes are capable of forming non-covalent interactions with each other, wherein these non-covalent interactions consist of A/T base pair interactions. The Action states that Nadeau et al. teach spacer entities that

consist of 2 A/T base pairs in combination with 5 G/C base pairs (reference, Example 3). However, such sequences are prone to the problem discussed in the present application; namely, the quenching or dequenching effects of G residues on FRET pair signal intensities (see present application, page 2, line 20 to page 3, line 3). The presence of the 5 G/C base pairs in the spacer entity in Nadeau et al. illustrates this problem. Looking at the Table in column 18, one can see that compared to the single dye pair arrangement, the 3-way junction exhibits a much higher pre-extension fluorescence intensity (3200 vs. 1300). The ratio of pre-extension fluorescence intensities (2.5; equal to 3200/1300) is much higher than the ratio of post-extension intensities (1.7; equal to 6800/4000), suggesting a dequenching effect of the G residues present in the spacer entity. The ratio of post-extension fluorescent intensity to pre-extension intensity of the 3-way junction (2.1; equal to 6800/3200) is much lower than that of the single dye pair arrangement (3.1; equal to 4000/1300). Therefore, although the absolute signal change is higher than in the case of the 3-way junction than in the case of the single dye pair arrangement, the signal/noise ratio (defined as the ratio of post-extension fluorescent intensity to pre-extension intensity) is lower for the 3-way junction.

In contrast, the presently claimed invention eliminates the unpredictable effects of G residues, by requiring that the spacer entity consist only of A/T base pairs. The meaning of this transitional phrase is well settled, as noted above. This element is neither taught nor suggested by Nadeau et al. Accordingly, reconsideration and withdrawal of the rejections of claims 1, 5, 10, and 27 under 35 U.S.C. 102(b) are respectfully requested.

Claim Rejections under 35 U.S.C. 103(a):

Claim 4 was rejected under 35 U.S.C. 103(a) as obvious over Nadeau et al. in view of Wittwer et al. (US Patent No. 6,140,054). Claims 6 and 7 were rejected as obvious over Nadeau et al. in view of Fisher (US Patent No. 6,054,568). Claims 8 and 9 were rejected as obvious over Nadeau et al. in view of Acton et al. (US Patent No. 6,228,581). Claim 14 was rejected as obvious over Nadeau et al. in view of Urdea et al. (US Patent No. 5,635,352). Claim 15 was rejected as obvious over Nadeau et al. in view of Ahern (The Scientist). The rejections are respectfully traversed.

While not admitting to the propriety of the rejection, and solely to expedite prosecution of the application, Applicants have chosen to amend claim 1 to recite that the spacer entities of the FRET hybridization probes are capable of forming non-covalent interactions with each other, wherein these non-covalent interactions consist of A/T base pair interactions. As noted above, Nadeau et al. neither teaches nor suggests this element

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of the claims as amended. Furthermore, none of the other references cited in the Action teach or suggest this element either. Accordingly, reconsideration and withdrawal of the rejections of claims 4, 6-9, 14 and 15 under 35 U.S.C. 103(a) are respectfully requested.

Conclusion:

In view of the above, Applicants believe all claims now pending in this Application are in condition for allowance. Applicants hereby request a two-month extension of time for responding to the Office Action. The Commissioner is hereby authorized to charge the extension of time fee (large entity) under 37 CFR 1.17 to Account No. 50-0812. The Commissioner is further authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account No. 50-0812.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned directly at 510-814-2891.

Respectfully submitted,

Date: Jan. 16, 2007


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